UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,241	08/05/2003	Zhen Zhang	58369 (71699)	6657

21874 7590 11/02/2006

EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/635,241	ZHANG ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *112-224* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-153, 157-158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *1 copy*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 119, 121-122, 125-126, 128-130, 135-136, 140, 154-156, 159-160, 162-164, 169-170, 174, 179, 193-195, 198-199, 201-203, 208-209, 213, and 218

DETAILED ACTION

.A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/28/2006 has been entered.

Claims 112-224 are pending.

Claims 1-111 are cancelled.

Claims 119, 121-122, 125-126, 128-130, 135-136, 140, 146, 154-156, 159-160, 162-164, 169-170, 174, 179, 191, 193-195, 198-199, 201-203, 208-209, 213, and 218 are withdrawn again from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claims. Election was made without traverse in the response filed 4/1/2005.

An action on the merits of claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-153, 157-158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224, as they read on the elected species, follows.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Claim Objections

Claim112 is objected to because of the following informalities: claim 112, as amended, recites a newly added limitation "wherein classification is."" The text of any added subject must

be underlined. 37 CFR 1.121. However, only the phrase "classification is" is underlined. Applicant is reminded to carefully review future amendments to ensure that they comply with 37 CFR 1.121.

Claim Rejections - 35 USC § 112

First Paragraph

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-148, 182-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 112 and 182, as amended, recite in steps (b) and (e) the limitation "wherein classification is a function of data elements values." Applicants point to page 31 of the specification for support for this limitation. The specification on page 31 discloses that quantification involves using a classification model. Classification models can be trained from known data elements that are pre-classified. The specification further discloses that data elements used to form the classification model can be referred to as a training data set or discovery data set. Once trained, the classification model can recognize patterns in data derived from data elements from unknown samples. Thus, the originally filed application does not

provide support for the limitation "a classification *is* a function of data elements values;" it is only discloses that classification models are used for quantification wherein the models recognize patterns derived from data elements.

New claims 222 and 224 recite the limitation "wherein the pattern recognition process comprises use of a classification model." Applicants point to page 31 of the specification for support for this limitation. The specification on page 31 discloses that "quantification involves using a pattern recognition process, such as a classification model." Therefore, "a pattern recognition process" does not USE a classification model, but IS a classification model.

For the reason stated above, the instant claims are rejected for introducing new matter.

Second Paragraph

Claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-153, 157-158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 112 recites in step (d) substep (iii) "the first samples and the second samples." The claim was previously rejected because the limitation ""the first samples and the second samples" was not clear. Applicants did not specifically address the rejection.

The examiner maintains that the limitation is still not clear for the reasons stated in the previous office action, and therefore the rejection of claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, and 147-148 is also maintained.

New claims 221-224 depend from claim 112, and therefore are also indefinite.

New rejections

Claim 112 recites in step (d) substep (iii) "the first samples and the second samples come from first and second populations." It is also unclear whether the first and second samples both came from first and second population OR the first samples come from the first population and the second samples come form the second population. As the intended limitation is not clear, claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, and 147-148, and 221-224 are indefinite.

Claims 112 and 182, as amended, recite the limitation "wherein classification is a function of data element value." It is not clear what limitation is intended because usually "classification" is performed by using a model and/or a variable which IS a function of data elements. Therefore, is not clear whether "classification" is intended to be a variable which is a function of data elements; a classification model that is described by a function which depends from data elements, *etc.* As the intended limitation is not clear, claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-148, 182-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224 224 are indefinite.

Claim 149 recites the limitation "to qualify each common data element … based on the ability … to classify a sample … as a function of data element value" in step (b). It is not clear whether the limitation "as a function of data element value" relates to the limitation "to qualify" or the limitation "to classify." As the intended limitation is not clear, claims 149-153, 157-158, 161, 165-168, 171-173, 175-178, and 180-181 are indefinite.

Claim Rejections - 35 USC § 103

Claims 112-117, 123-124, 127, 131-134, 137-139, 141, 143-145, 147-148, and 221-224 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin, *The Lancet*, 359:572-577 (February 16, 2002), in view of Golub, *Science*, 286:531-537 (Oct. 15, 1999).

Petricoin discloses analyzing two biological state classes – "unaffected" and "affected" wherein the affected group is known to have cancer. Petricoin discloses analyzing two independent sets of samples. Specifically, one "sample" is composed of 50 control samples for preliminary analysis, other 17 control samples, and samples from cancer patients for preliminary analysis (*see* p. 572-573, Methods and *Study Population*; table 1; fig. 1, p. 575, and p. 576). Thus, the analysis of the original test data is analysis of "the first set" of samples. A second "sample set" is composed of 50 control samples for the masked analysis, other unaffected samples, and benign disease control samples (p. 573-573; fig. 1, p. 575, and p. 576). Petricoin teaches that results from the test (masked data) may be added to the model/dataset to improve prediction (p. 576, right col., third full paragraph). Therefore, Petricoin discloses that both "samples" were collected and separately statistically analyzed to classify samples into different biological states (*e.g.*, cancer and unaffected states) (fig. 1, p. 575, table 2, p. 576, left col.) AND also discloses an "intersection" subset (the totality of the data used for classification after "improvement"). Also, the results obtained from two independent samples (preliminary and masked) were "intersected" wherein data elements (key values for classifying samples, *e.g.*, M/Z) in the intersection subset is a member of both subsets (preliminary and masked samples) (p. 576). Petricoin teaches selecting a first subset of data elements from the first data (key M/Z values) (fig. 1 and p. 575 and 576). Petricoin further discloses a preanalytical variable, *e.g.*,

medical status, a clinical characteristic, medical condition (*e.g.*, premenopausal, menopause, age, benign diseases, *etc.*) and age distribution (*see* table 1, p. 573, p. 576). Petricoin discloses samples collected at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p. 575, left col.). Petricoin discloses reshuffling (resampling) of the two highest rated sets to form new subset candidates (p. 575). Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation data set (masked serum samples, p. 575 and p. 577). Petricoin discloses a biological state is a characteristic of presence of a disease (cancer) and a biomarker is a diagnostic of a disease (CA125). Petricoin teaches that values of data elements represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z values determined by MS, p. 573; see also peaks on fig. 2). Expression of a law-molecular-weight protein (a cancer antigen CA125) is measured by coupling serum samples with a C16 hydrophobic interaction protein chip array (an immobilized capture affinity array) and the amount of the protein is measured by SELDI-TOF mass spectrometry (p. 573, right col.). The sample of Petricoin is serum and data collected from serum relate to the cellular localization of components in a sample (*e.g.*, components located in a soluble cell fraction or "attached" to suspended cell membranes) (p. 573, left col.). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p. 575, left col.). Petricoin also discloses "pattern-recognition" (p. 576, right col., third full paragraph, line 10). Petricoin discloses a "classification" as a pattern recognition process (fig. 1; p. 575, left col.).

Petricoin does not specifically teach selecting a second subset and displaying the intersection subset.

Golub discloses a method for classifying cancer by using gene expression monitoring (p. 531). Golub discloses using two classes (ALL and AML acute leukemia) and two samples comprising both classes (38 initial leukemia samples and independently collected 34 leukemia samples) (p. 532, 534). Golub discloses selecting "predictors" from the first sample (38 samples) and testing the predictors on an independent 34 leukemia samples (p. 532). Golub further discloses prediction strengths for both the initial (cross-validation) sample and an independent sample and selection of data elements with high prediction strength for both samples (selecting a first and a second subset) (p. 543 and fig. 3). Golub also discloses comparing two samples wherein the structure (data elements – gene predictors) in the initial sample is also seen in the independent sample (*i.e.*, samples are intersected) (p. 534, middle col. and fig. 4). Golub discloses displaying the intersection (fig. 3). Golub discloses that different types of samples, bone marrow and blood, were collected by different protocols (*e.g.*, samples from SJCRH were processed with a very different protocol) (p. 536-537, paragraph 23). Also, collection of bone marrow and blood requires different protocols. Golub discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to select both a first and a second subset of data elements and display the intersection, as taught by Golub, where the motivation would have been to test a model/hypothesis and to compare results from a model and a test, as taught by Golub, p. 534.

Answer to arguments

Applicants argue that Golub teaches away from the instant method where data sets may be collected by different collection protocols. Applicants further argue that Golub does not disclose selecting an intersection subset. Applicants' arguments have been considered, but are found not persuasive.

As set forth in the previous office action, Golub discloses a range of samples, *e.g.*, bone marrow and peripheral blood samples, samples collected from children and adults, samples collected from different labs, and samples collected by different protocols (p. 532, right col., last paragraph). Although Golub states that the average prediction strength was lower for samples from one laboratory that used a very different protocol for sample preparation and suggests standardization of sample preparation, Golub does teach using different sample preparation protocols (p. 532, right col., last paragraph). Thus, the examiner maintains that Golub discloses that data sets may be collected by different collection protocols and selecting an intersection subset, and therefore the instant rejection is also maintained.

Claims 118, 120, 142, 149-153, 157-158, 161, 165-168, 171-173, 175-178, 181-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-220 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin, *The Lancet*, 359:572-577 (February 16, 2002), in view of Golub, *Science*, 286:531-537 (Oct. 15, 1999), as applied to claims 112-117, 123-124, 127, 131-134, 137-139, 141, 143-145, 148, and 221-224 above, and in view of Barnhill, U.S. Patent 6,789,069.

Petricoin and Golub make obvious claims 112-117, 123-124, 127, 131-134, 137-139, 141, 143-145, 148, and 221-224, as set forth above.

Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and processing experimental data and bioinformatics software for processing data (p. 573 and 575). Petricoin discloses a computer based chip system (the Protein Biology System 2 SELDI-TOF mass spectrometer such as Ciphergen Biosystems with a detector and a chip reader, p. 573). Petricoin also discloses that data were collected and were used later for analysis (*i.e.*, data are stored).

Petricoin and Golub do not disclose a supervised learning algorithm and specifically, a support vector machine analysis; protein binding partners in an expression profiling assay; and a computer system and a computer readable medium for performing the method.

Barnhill discloses a method for classifying unknown samples using a learning machine, similar to that of Petricoin. Barnhill discloses different methods for data acquisition such as nucleic acid arrays and protein expression assays (*e.g.*, antibody chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col, 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (*see* for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a

memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a supervised learning algorithm and specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre-and post-processing data and maximize the value of genomic and proteomic information, as taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 – col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Answer to Arguments

Applicants argue that Barnhill does not disclose using two separate samples and selecting an intersection subset.

This is a rejection under 35 U.S.C. 103(a) over a combination of references. Although Barnhill discloses two independent samples (training and test samples, col. 50), Barnhill is relied

upon for the limitations disclosed in claims 118, 120, 142, 149-153, 157-158, 161, 165-168, 171-173, 175-178, 181-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-220, for the same reason as set forth in the previous office action mailed 5/19/2005 for claims 3, 5, 29, 36-38, 40, 44-45, 48, 53-56, 59-61, 63-67, 71-79, 81, 85-86, 89, 94-97, 100-102, and 104-108. Petricoin and Golub teach an intersection subset and other limitations of the method of claim 112, as set forth above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE A. MORAN
PRIMARY EXAMINER

10/26/06